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How to Reduce Waste and Costs in Clinical Trial Supply

Knowledge Sharing Series

How to Reduce Waste and Costs in Clinical Supply

Abstract

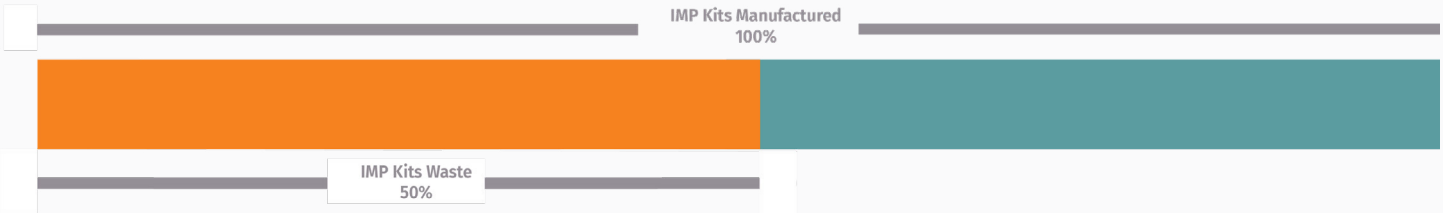
Reducing investigational medicinal product (IMP) waste and distribution costs without increasing the risk of missed patient visits due to inadequate site stock is a challenging optimization task. However, the evolution of software tools are providing supply managers with more options to push the boundary on what can be achieved:

Modern RTSM platforms can automate the site buffer management process and thus substantially reduce the risk of sites being undersupplied. In addition, site resupply long windows can be optimized using modeling-in-demand forecasting solutions. Beyond site resupplies, modern RTSM platforms can also dynamically calculate the trigger and resupply quantities for each kit type at each depot. With these values, supply managers no longer have to overstock depots to prevent depot stockouts, but can instead trigger depot shipments when necessary, as well as ensure that depot shipments occur in the desired frequency. Finally, demand forecasting solutions, that support data integration from the RTSM, automation, alerting can be used not only to identify an optimal IMP supply plan during the study setup phase but also to ensure that this supply plan remains optimized throughout the trial.

Introduction

With the cost of conducting clinical trials ever on the rise, the need for cost control is steadily increasing. While clinical trial supply usually doesn't feature high on the overall cost-controlling agenda, the pressure to reduce costs in this space is also growing. Among other causes, the increase in IMP supply costs is undoubtedly related to an increase in average unit costs caused by the rapidly expanding use of biologicals, as well as the rising costs for the corresponding comparators.

Nevertheless, there is little indication to date that trial sponsors are succeeding in making a significant dent in some of the most important cost drivers in clinical trial supply: IMP waste and IMP distribution costs. Instead, mean waste was reported in 2021 to be hovering at a disturbing 50%, which begs the question if there aren't measures available that can improve on this while keeping the crucial aspect of supply security front and center.



Kachwala, M., Kilgore, C., Kinscher, K., & Talwar, V. (2021, November 29). Clinical supply chains: How to boost excellence and innovation. McKinsey & Company.

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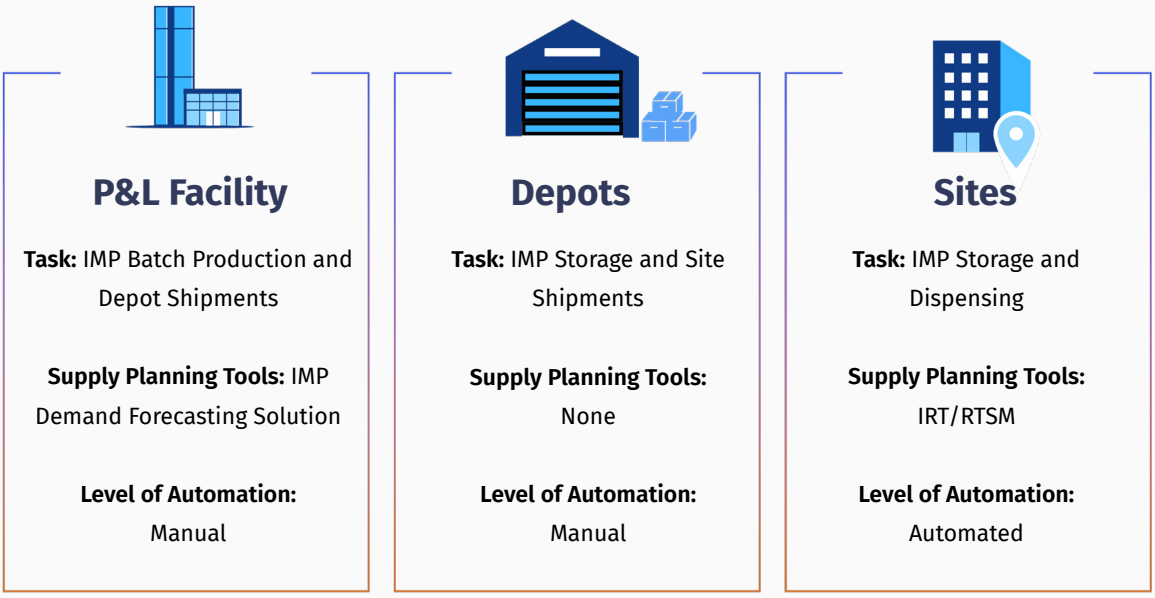
Scope

In a somewhat simplified model, the clinical trial supply chain begins with the packaging and labeling of IMP batches at a P&L facility and continues with shipment to clinical depots, where the IMPs are stored and later sent to replenish the inventory at clinical trial sites. At the sites, the IMPs are stored again and finally dispensed to clinical trial participants according to their specific patient journey needs. In terms of supportive technology for this supply chain, there is surprisingly little. Supply planning can be supported by demand forecasting solutions, which model the IMP demand for an entire study (or the remainder of the study), but the adoption of these tools is far from universal. By contrast, the planning of shipments to depots is rarely supported by technology at all. Instead, the more common approach is that supply managers manually decide when depot resupply shipments are triggered and how many units (kits) a depot shipment contains. Other than depot resupply shipments, the planning of IMP shipments from depots to clinical trial sites is commonly managed by randomization and trial supply management (RTSM) software as an automated, daily task.



Model of the outbound IMP supply chain. IMPs are packaged and labeled at the packaging and labeling (P&L) facility, distributed to depots and then sites and finally dispensed to patients. IMP demand and supply forecasting solutions and the IRT/RTSM are the most relevant supply planning technologies, but many aspects of supply planning still remain essentially manual tasks.

In this model, there are three key opportunities for introducing measures to optimize the IMP supply chain: site shipment planning, depot shipment planning and supply planning. Let's look at each one to determine what practical optimization steps can be taken.

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Site Shipment Planning

Because site resupply shipments are planned and created automatically by the RTSM, optimizing the planning of site resupply shipments means reviewing the RTSM's site resupply algorithm in search of optimization potential.

Irrespective of the RTSM platform or vendor, the site resupply algorithm always works in fundamentally the same way by using a two-step algorithm that first decides whether a shipment should be triggered and then determines how many kits should be resupplied. The trigger algorithm determines the safety stock and is thus focused on risk mitigation. To achieve this objective, the trigger algorithm forecasts the maximum demand of each kit type at each site in the time it could take for a resupply to reach that site (maximum site shipment lead time, short window) and creates a site resupply shipment if the inventory of one or more kit types is less than the maximum demand in the short window.

In contrast to the trigger algorithm, the resupply algorithm is not focused on mitigating the risk of missed visits but instead on achieving a healthy balance between resupply shipment size and resupply shipment frequency. To achieve this, the resupply algorithm forecasts the average demand in the long window, a defined number of days after the end of the short window. A large long window will cause larger resupply shipments, higher site stocks and, consequently, higher IMP waste, but also savings through a lower resupply shipment frequency, while a smaller long window will have the opposite effect.

In the RTSM site resupply algorithm, forecasted demand is either predictable or unpredictable. For example, the demand forecasted for a randomized patient with a known dose level and weight is typically predictable, while the forecasted demand for a patient who is currently in screening is typically unpredictable because it depends on the treatment arm the patient has yet to receive. Currently, most RTSM platforms only forecast predictable demand and require the user to cover unpredictable demand with manually defined and maintained buffer stocks. This practice is well accepted, but supply managers often manage hundreds or even thousands of clinical trial sites across multiple trials, so keeping the buffer settings aligned with the unpredictable demand forecast at all of these simultaneously is a highly challenging task. Buffer settings that are too high overestimate the unpredictable demand and cause overstocking of clinical trial sites, while buffer settings that are too low underestimate unpredictable demand and therefore cause missed visit risks. In contrast to the industry standard, there are some RTSM platforms that employ a probabilistic forecasting algorithm to support unpredictable demand forecasting.

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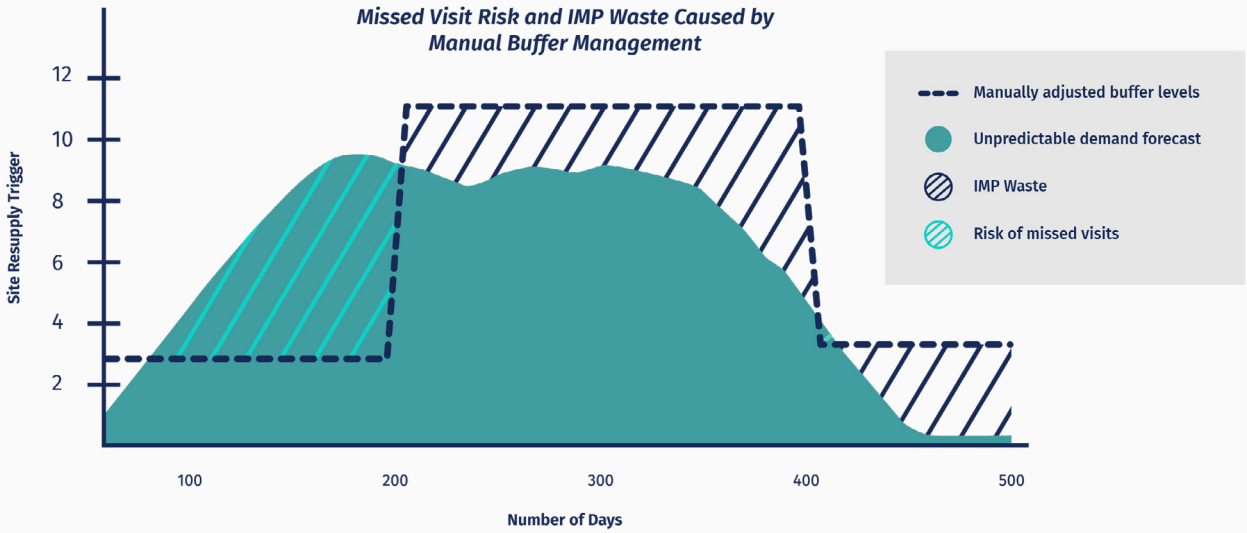
These RTSM platforms are more complex and therefore more challenging to work with, but effectively calculate the optimal buffer settings for each kit type at each site on each day and thus overcome the challenges associated with manual buffer management. To improve the balance between risk and cost, it is advisable to leave unpredictable demand forecasting to the RTSM site resupply algorithm.



Manual buffers vs. unpredictable demand forecast. Manually managed site buffer levels remain unchanged until manually updated, while an unpredictable demand forecast changes as the trial evolves at each site. Days where the manual buffer level is below the unpredictable demand forecast are associated with an increased risk of missed visits, while days where the manual buffer level is above the unpredictable demand forecast are associated with an increase in IMP waste.

It should be noted that unpredictable demand forecasting algorithms haven't been around for a very long time and are still evolving. Therefore, trial sponsors should have an interest in collaborating with RTSM vendors to further improve unpredictable demand forecasting algorithms.

In addition to choosing an RTSM that supports unpredictable demand forecasting, attention should be given to defining and maintaining the long window for site resupplies. As noted above, the long window can be used to alter the balance between IMP waste and site shipment costs. It's not always easy to predict exactly how the balance will change over different long window settings, but demand forecasting solutions such as those used for IMP batch planning, are quite good at modeling this process and can thus be used to identify long window settings that represent a desired balance between IMP waste and distribution cost.

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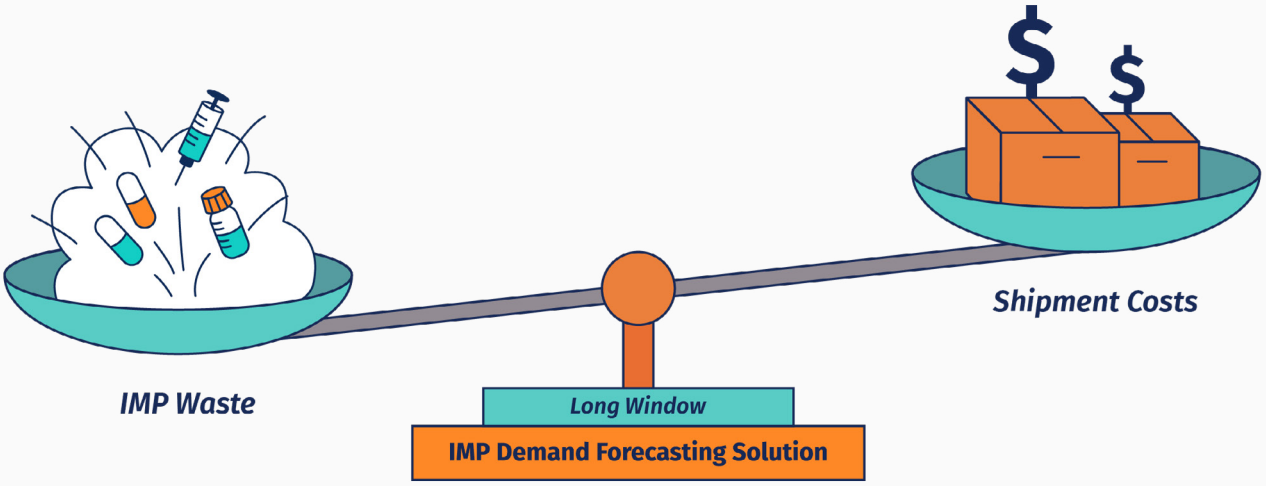

Site long window demand optimization. IMP demand forecasting solutions are used to determine the long window setting which represents an optimal balance between IMP waste and distribution shipment costs. Large long window settings cause fewer, larger site resupply shipments and hence more IMP waste, but lower distribution costs, while smaller long windows cause less IMP waste and higher distribution costs.

Depot Shipment Planning

As discussed above, depot shipment planning is still largely a manual task in most studies, which can be quite challenging for supply managers who are responsible for managing the resupply of multiple depots in multiple studies. Therefore, it's not surprising that the tendency is to err on the side of safety by overstocking depots to mitigate depot stock-out risks, even if this means increasing IMP waste.

Given that the RTSM has a lot of the information that would be needed to forecast depot demand, it is fair to argue that this should be how depot demand is forecasted, but traditional RTSM platforms don't support this feature. One major reason is that traditional RTSM platforms, who, as discussed above, rely on manual buffers, are missing a critical puzzle piece needed to forecast depot demand, because the depletion and replenishment of manually defined site buffers can't be forecasted. By contrast, RTSM platforms which forecast unpredictable demand dynamically instead of relying on manual site buffers can forecast depot demand quite accurately by aggregating the demand from sites supplied by a depot and there are RTSM platforms which support this feature.

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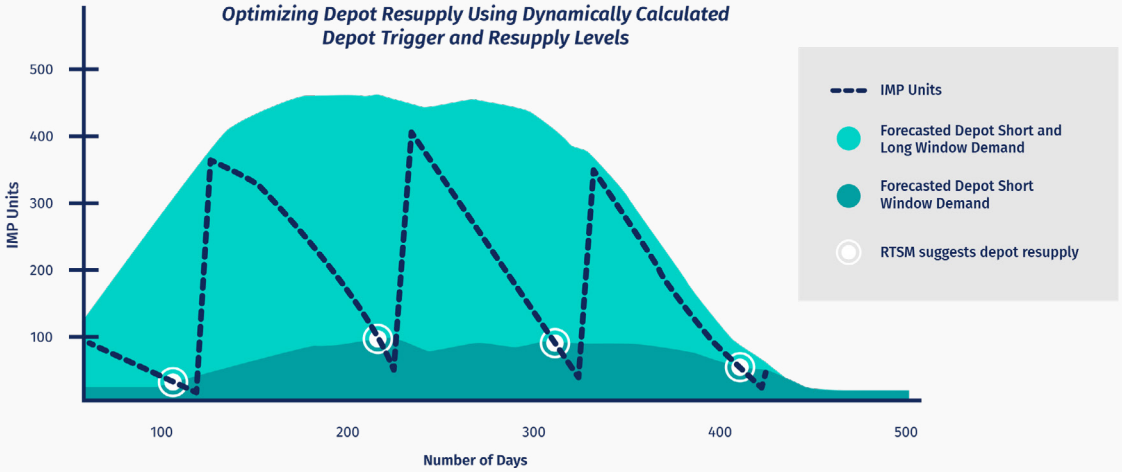
To forecast the demand at a depot, the RTSM leverages the existing information on patients and site inventories together with the site resupply algorithm to forecast site resupplies to all the sites supplied by that depot. If the depot inventory is less than the maximum forecasted demand for site resupplies in the time it could take to resupply the depot (depot short window), then the RTSM alerts the supply manager that a depot resupply is needed. If a depot resupply is triggered by the supply manager, the RTSM forecasts the average demand for site resupplies in a defined depot long window to propose the depot resupply shipment quantities.

With support from the RTSM, the supply manager can wait to resupply depots until the depot stock is depleted to the logical trigger level (maximum depot demand in the maximum depot resupply shipment lead time) and resupply in quantities that lead to a planned and desired depot resupply interval (depot long window). This is an effective method of decreasing IMP waste while at the same time not compromising IMP supply security.



Optimized depot resupply. Depot resupplies are triggered when the depot inventory is depleted to a dynamically computed depot resupply trigger (Depot Short Window (SW) Demand) which corresponds to the maximum depot demand in the maximum depot shipment lead time and depot stocks are replenished to a dynamically computed replenish-to level which corresponds to the trigger level plus the average depot long window demand (Depot SW + Long Window (LW) Demand).

IMP Supply Planning

The plan (quantity, timing) for the packaging and labeling of IMP batches to supply the participants in a clinical trial is initially created during the study planning phase. The increasing use of IMP demand forecasting solutions has seen a substantial growth of technological support for this process and has helped improve the balance between risk and cost in the IMP supply. For this to work efficiently, it is essential that the supply planning process begins early in the trial planning phase, ideally before the protocol is finalized. In this case, the demand forecasting solution can be used to quantify the benefit of optimization measures, allowing the study team to make an educated decision whether the measure should be adopted or not.

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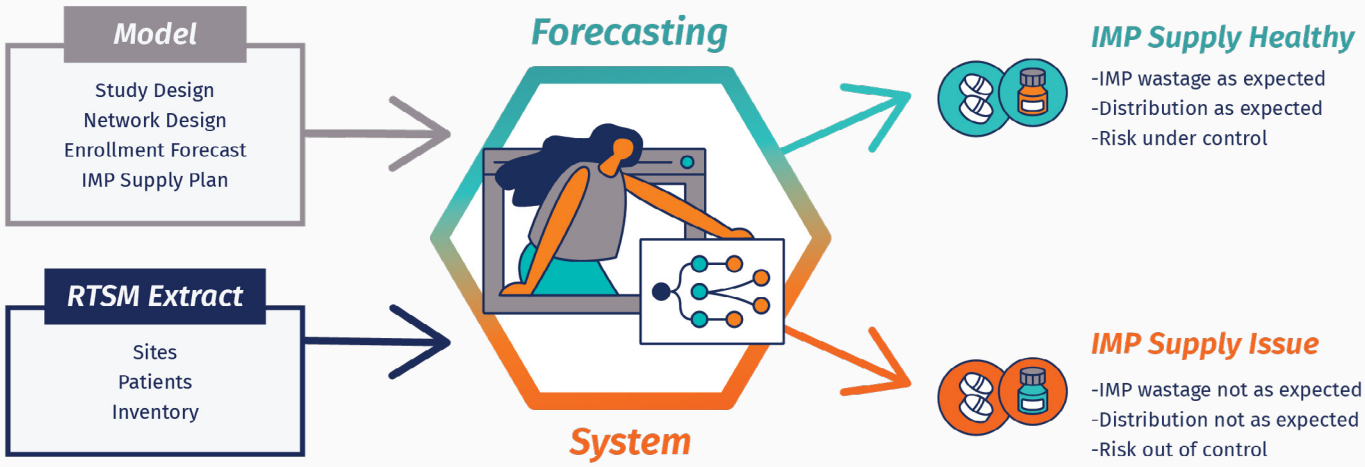
For example, stratification by depot region can cause a significant reduction of IMP waste in some trials and quantifying the value of such a measure by modeling a corresponding what-if scenario in a demand forecasting solution can go a long way to help drive the decision whether introducing stratification by depot region is worthwhile.

Once the trial begins, it's common that the assumptions upon which the initial IMP supply plan were based (e.g. enrollment forecast, screen failure rate, dropout rate) don't turn out to be accurate. Therefore, it is critical that the IMP supply plan be reviewed and revised according to the evolution of the clinical trial. Currently, this involves integrating the RTSM data into the demand forecasting solution and forecasting the IMP demand and supply for the remainder of the trial. This task is cumbersome and therefore not often performed with high frequency, leading to IMP supply plans that are often based on outdated data.

A more efficient approach is to introduce automation into the re-forecasting process, such that the forecast occurs as a regular (daily, weekly) scheduled task based on the study design (model), the current IMP batch plan, the current enrollment plan, and the latest data from the RTSM and returns a forecast report with indicators for risk and cost. If these indicators are used to trigger alerts when an indicator trends out of or leaves an expected corridor, then the re-forecasting process is fully automated and only requires supply managers to react when they receive an alert. In this case, optimization measures can be identified and assessed in what-if scenarios, very similarly to the optimization process employed during study planning and resulting in an updated optimized IMP supply plan. When the updated plan has been identified, this replaces the previous plan, and the automated re-forecasting cycle begins again.



Automated monitoring of IMP supply plan health. At regular (daily, weekly) intervals, an IMP demand and supply forecast is generated for the remainder of the trial based on the study design, the network design, the current enrollment forecast, the current IMP supply plan and the current RTSM extract data to determine whether the risk and cost of the IMP supply in the trial are under control. If the risk or cost are outside or trending outside an expected corridor, then an alert is sent to the supply manager.

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With this approach, the IMP supply plan can be maintained in an optimized status throughout the lifecycle of the clinical trial, thus contributing to the best possible balance of risk and cost in the IMP supply of a clinical trial.

Conclusion

Fully optimizing the balance between the risk of missed patient visits due to inadequate site stock and costs due to IMP waste and distribution shipments will never be fully achieved, but there are still measures available to make substantial progress toward this objective, which can be considered as low-hanging fruit:

RTSM platforms that support unpredictable demand forecasting can overcome the issues associated with manual site buffer management and thus significantly reduce the risk of missed visits. Demand forecasting solutions can be used to optimize long window settings by modeling the impact of different long window settings on the balance between IMP waste and distribution costs. As a major step toward reducing IMP waste at depots, RTSM platforms that support unpredictable demand forecasting can dynamically calculate trigger and resupply quantities for each kit type at each depot, giving supply managers much-needed visibility of the forecasted depot demand. This ensures that depot shipments are triggered no earlier than necessary, as well as facilitating that depot shipments occur in an optimized frequency. Finally, demand forecasting solutions that support data integration from the RTSM, automation and alerting can be used to not only identify an optimal IMP supply plan during the study setup phase, but also to ensure that this supply plan remains optimized throughout the trial.

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Meet the **Author**

Benjamin Etschmann holds a PhD in veterinary medicine and has spent 15 years in clinical trial supply management in various roles, including operational trial supply logistics management and trial supply setup management. However, his primary focus has been in IVRS/IRT/RTSM management and demand forecasting using dedicated stochastic simulation tools. In his current role, he consults clients and internal teams on probabilistic site and depot demand forecasting in IVRS/IRT/RTSM.

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